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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,779	DUDICH ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-8 and 10-22* is/are pending in the application.

4a) Of the above claim(s) *4,11-13,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5-8,10,14-19 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on July 13, 2007 is acknowledged. Substitute Specification filed on April 08, 2005 is acknowledged. Claims 1 and 9 have been cancelled and new claim 14 was added. Claims 2-8, 10-22 are pending in this application.

Restriction

1. Applicant's election of Group 2 (claims 2-8 and 16-21), drawn to a cyclic peptide and the election of species of structure claimed in claim 18 in the reply filed on July 13, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However, since the base claim has been amended to a cyclic peptide structure, the first method, a method for suppressing apoptotic regulatory pathways in human and animal cells by treating the cells with peptide structures according to the base claim.

2. Thus, the requirement is still deemed proper and is therefore made FINAL. Claims 4, 11-13 and 20-21 are withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected invention, there being no allowable generic or linking claim. A search was conducted on the elected species and this appears to be free of prior art. The search was extended to broad generic claim 2. Claims 2-3, 5-8, 10, 14-19 and 22 are examined on the merits in this office action.

Rejection-35 U.S.C. 112, 2nd

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2, 7, 8 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

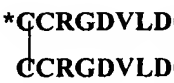
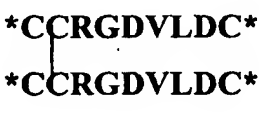
5. Claim 2 recites a cyclic peptide structure with a general formula $CCRGDVLD_nX_mY$, wherein X is any hydrophobic amino acid, and Y is any hydrophilic amino acid. It is unclear how the general formula above would be able to form a cyclic peptide structure. The only C residues are the C as position 1 and position 2.

6. Claim 7 recites "the peptide structure according to Claim 2, wherein X in the general formula means V, L or W, X_m may contain any combination of V, L and W and Y means D, E, or G". The phrase "X_m may contain any combination of V, L and W" is unclear since X_m in claim 2 is defined as an "X" and an "m" as two separate variables, wherein m is 1, 2 or 3. Therefore, X_m cannot be "any combination". For example, when m is 1, X is either V, L or W. Thus, X_m cannot be any combination of V, L and W.

7. Claim 7 recites "the peptide structure according to Claim 2, wherein X in the general formula means V, L or W, X_m may contain any combination of V, L and W and Y means D, E, or G". It is unclear how a peptide having the sequence $CCRGDVLD_n[(V)(L)(W)][(D)(E)(G)]$ would form a cyclic peptide.

8. Claim 8 recites the limitation "peptide structure further defined as C*C*RGDVLDC*" in the 2nd line of the claim. There is insufficient antecedent basis for

this limitation in the claim. The peptide structure C*C*RGDVLDC* appears for the first time in claim 8, since claim 2 recites the peptide structure $CCRGDVLD_nX_mY$.

9. Claim 19 recites the peptide structure  and that this is a cyclic dimer. It is unclear how this structure can be cyclic, since the only structural evidence of the structure provides is a "dimer". Furthermore, the structure dimer bonding is unclear. It is unclear whether the C-C bond is formed from the 1st C of the 1st peptide to the 1st C of the 2nd peptide or C-C bond is formed from the 2nd C of the 1st peptide to the 2nd C of the 2nd peptide, since the specification and Figure 1 appears to show the peptide structure  .

Rejection-35 U.S.C. 112, 1st

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 2-3, 5-8, 10, 14-19 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

12. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

13. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

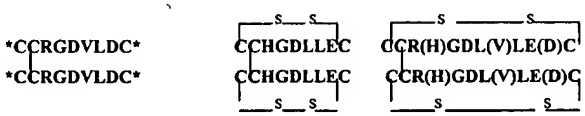
"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

14. The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative. number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

15. In the instant case, the claims are drawn to a cyclic peptide structure with a general formula of $CCRGDVLD_nX_mY$, in which formula X is any hydrophobic amino acid and Y is any hydrophilic amino acid, and the index n is 1, 2 or 3 and index m is 1, 2, or 3. The generic statement general formula of $CCRGDVLD_nX_mY$ does not provide ample written description for the compounds since the claims do not describe the invention being claimed. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

16. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 2 is broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limited to peptides

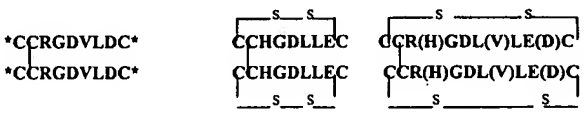
consisting of CCRGDVLD$_n$X$_m$Y structures. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule, peptidomimetics or other peptidic molecules, and other synthetic peptide or peptide-like molecule that can be cyclized.

17. The specification is limited to the peptides *Cys-Cys-Arg-Gly-Asp-Val-Leu-Asp-Cys* (SEQ ID NO: 1), Arg-Gly-Asp-Val-Leu-Asp (SEQ ID NO: 2), His-Gly-Asp-Leu-Leu-Glu (SEQ ID NO: 3), *Cys-Gly-Arg-Gly-Asp-Val-Leu-Asp-Cys* (SEQ ID NO: 4), *Cys-Cys-His-Gly-Asp-Leu-Leu-Glu-Cys* (SEQ ID NO: 5), *Cys-Gly-His-Gly-Asp-Leu-Leu-Glu-Cys*, and 

(see specification pages 8-22). These structures and sequence imply that X must be a "C" residue or both X and Y are absent. The specification does not disclose the peptide structures claimed in the

base claim 2. For example, $CCRGDVLD_nX_mY$ implies that X and Y must be present in the structure. There are many possible different structures that the peptide of claim 2 can form: (1) CCRGDVLDXY, (2) CCRGDVLDDXY, (3) CCRGDVLDDDXY, (4) CCRGDVLDXXY, (5) CCRGDVLDDXXY, (6) CCRGDVLDXXXY, (7) CCRGDVLDDXXXY, (8) CCRGDVLDDDXXXY and so on. The least the amount of amino acids that can be present is 10 and the most is 14. Furthermore, claim 3 recites that the peptide structure has 0, 1, 2, or 3 flanking cysteine residues at the N-terminus and 0, 1, 2, or 3 flanking cysteine residues at the C-terminus of the peptide. Thus, before the C1, there may be up to 3 more C residues on the N-terminus and after the Y residue, there may be up to 3 C residues on the C-terminus. For example for (1) above, the structures could be (1a) CCRGDVLDXY, (1b) CCCRGDVLDXY, (1c) CCCCRGDVLDXY, (1d) CCRGDVLDXYC, (1e) CCRGDVLDXYCC, and so on. Claim 7 recites that X means V, L or W, and Y means D, E, or G. However, the specification does not describe any peptide structures that consist of X and Y residues on the structure. The peptide structures described consist of both X and Y missing in the structures. There is no limitation of X and Y being absent from the structures. Furthermore, the specification does not disclose how and where the cyclization occurs on the peptide structure. The specification describes di-sulfide bonds being formed from Cysteine to Cysteine residue (C2 to C2 of the dimer, C1 to C9 of the dimer, C2 to C2, C1 to C9 and C1 to C9 of the dimer) (see specification pages 8-22). However, the specification does not describe how the cyclization occurs between residues C1 to R3 or from any of the other amino acid residues on $CCRGDVLD_nX_mY$ structures.

Cyclization can occur from any functional groups of any amino acid residues, depending on the secondary structure and the peptide lengths. Description of *Cys-Cys-Arg-Gly-Asp-Val-Leu-Asp-Cys* (SEQ ID NO: 1), Arg-Gly-Asp-Val-Leu-Asp (SEQ ID NO: 2), His-Gly-Asp-Leu-Leu-Glu (SEQ ID NO: 3), *Cys-Gly-Arg-Gly-Asp-Val-Leu-Asp-Cys* (SEQ ID NO: 4), *Cys-Cys-His-Gly-Asp-Leu-Leu-Glu-Cys* (SEQ ID NO: 5), *Cys-Gly-His-Gly-Asp-Leu-Leu-Glu-Cys*, and



are not sufficient to encompass numerous other peptide structures that are claimed. As described above, there are numerous possibilities that the peptide structure must form: (1) CCRGDVLDXY, (2) CCRGDVLDDXY, (3) CCRGDVLDDDXY, (4) CCRGDVLDXXY, (5) CCRGDVLDDXXY, (6) CCRGDVLDXXXY, (7) CCRGDVLDDXXXY, (8) CCRGDVLDDDXXXY and so on. There is no examples or support provided to encompass the numerous characteristics of the whole genus claimed.

18. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

19. Claims 10, 14-19 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature or the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (5) the breadth of the claims:

The claims are drawn to a cyclic peptide structure with a general formula of $CCRGDVLD_nX_mY$, in which formula X is any hydrophobic amino acid and Y is any hydrophilic amino acid, and the index n is 1, 2 or 3 and index m is 1, 2 or 3, said peptide structure having a capability to regulate apoptotic cell death. Because claim 2 recites a

peptide structure index m and n are 1, 2 or 3, and claim 3 recites that 0, 1, 2, or 3 C residues flank N-terminus and 0, 1, 2 or 3 C residues flank C-terminus of the peptide, this reads that the peptide structure comprises between 10 to 20 amino acids.

(2) The state of the prior art and (4) the predictability or unpredictability of the art:

With regards to the effect of amino acid substitution in a peptide or protein, the art is unpredictable.

Rudinger (Peptide Hormones, JA Parsons, Ed., 1976, 1-7) teaches that, "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted a priori but must be determined from case to case by painstaking experimental study" (see p. 6). Additionally, SIGMA states that with regards to design of peptide sequences that, "Even for relatively short sequences, there are essential and non-essential (or less important) amino acid residues, although the relative importance of the individual amino acid residues is not always easy to determine" (see p. 1). SIGMA further describes what effect some substitutions may have, rather than what effect they will have on hydrophobicity, secondary structure (which will affect tertiary and quaternary structure), and solubility.

With regards to prediction of the native conformation of a protein (structure), the art is unpredictable. Berendsen (Science, 1998, 282: 642-643) states, "The prediction of the native conformation of a protein of known amino acid sequence is one of the great open questions in molecular biology and one of the most demanding challenges in the

new field of bioinformatics" (see p. 642). Furthermore, Berendsen states that "Folding to the stable native state [computationally] has not (yet) occurred, and the simulations do not contain any relevant statistics on the process. The real protein will fold and refold hundreds to thousands of times until it stumbles into the stable conformation with the lowest free energy. Because this hasn't happened (and couldn't happen) in the simulations, we still cannot be sure of the full adequacy of the force field" (see p. 642).

Further, the effects of a single amino acid substitution can have substantial effects on proteins in structure and/or function and are exemplified by the difference between hemoglobin (Hb) and abnormal hemoglobins, such as sickle-cell hemoglobin (HbS). Voet et al teaches that the mutant hemoglobin HbE [GluB8(26)β to Lys] has, "no clinical manifestations in either heterozygotes or homozygotes" (see p. 235). Further, Hb Boston and Hb Milwaukee both have single point mutations which results in altered binding affinity and ineffective transfer from the Fe(III) to Fe(II) oxidation state. Conversely, a single point mutation in Hb Yakima results in increased oxygen binding by the heme core, and in Hb Kansas, the mutation causes the heme center to remain in the T state upon binding oxygen (rather than structurally rearranging to the R state) (see p. 236). Further, HbS is a single point mutation, Val to GluA3(6)β (see p. 236), which results in deformation and rigidity of the red blood cell. The mutation also provides protection against most malarial strains.

Given that one could not determine the structure of a protein computationally, and that the effect of amino acid substitution is unpredictable, it flows logically that one would be unduly burdened with experimentation to determine the effect of amino acid

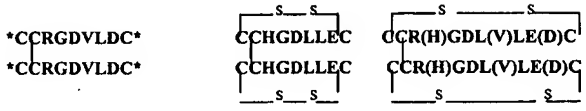
substitution(s) in a peptide or protein, with regards to structure, function, or physical/chemical properties. Therefore, making any peptide having at least 18 amino acids that has the same activity as the claimed peptide, one would be unduly burdened with experimentation to determine the effect of amino acid content, substitution(s), addition and deletions in a peptide or protein, with regards to structure, function, or physical/chemical properties.

(3) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples:

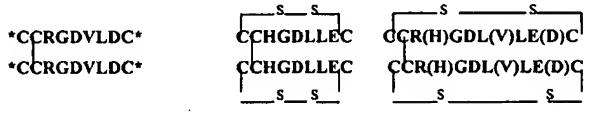
The specification is limited to the peptide or peptide-like molecules that belong to the same class of protein, alpha-fetoprotein (AFP). The specification discloses that multiple evidences of AFP-mediated tumor cell growth suppression have been reported, but the active site of the AFP molecule that is responsible for apoptosis signaling has not been identified (see p. 3, lines 27-29). Additionally, the specification discloses that the important integrin binding site is a tripeptide Arg-Gly-Asp (see p. 4, line 17). The working example describes the peptides *Cys-Cys-Arg-Gly-Asp-Val-Leu-Asp-Cys* (SEQ ID NO: 1), Arg-Gly-Asp-Val-Leu-Asp (SEQ ID NO: 2), His-Gly-Asp-Leu-Leu-Glu (SEQ ID NO: 3), *Cys-Gly-Arg-Gly-Asp-Val-Leu-Asp-Cys* (SEQ ID NO: 4), *Cys-Cys-His-Gly-Asp-Leu-Leu-Glu-Cys* (SEQ ID NO: 5), *Cys-Gly-His-Gly-Asp-Leu-Leu-Glu-



Cys*, and (see specification pages 8-22).

The working example only describes the peptide structures that are 9 amino acids, 6 amino acids, a dimer of 18 amino acids, and cyclic peptides with 18 amino acids in lengths. Example 1 discloses that the peptides were synthesized with a synthesizer Model 430A, and for SEQ ID NO: 1, 9-mer peptide corresponds to the 251-259 amino acid sequence of the human AFP, and the second cysteine is capable of formation of the S-S bond between two adjacent cyclic monomeric peptides (see p. 12, lines 20 and 25-29). Example 1 also discloses that SEQ ID NOs: 4, 2, 5, 6 and 3 (see p. 13, lines 1-22). Example 3 discloses that cyclic peptide from AFP apocyclin-A (SEQ ID NO: 1) abrogated AFP-induced apoptosis in U-937 cells (see Figure 2). Example 4 discloses that apocyclin-A (SEQ ID NO: 1) inhibits anti-Fas-induced apoptosis in U-937 cells in vitro (see Figure 3). Example 5 indicates that the Cys_{252} is functionally important amino acids in the active site of the AFP molecule and its substitution to Gly completely abrogates ability of the peptides to interact with apoptotic activity of the entire AFP molecule (see Example 5 and Figure 4). Examples 6 and 7 indicate the synergistic effect of apocyclin-A with low doses of endogenous cytochrome c. Examples 8 and 9 indicates the inhibition of the cytochrome c/AFP-mediated caspase activation. Example 10 discloses the preparation of anti-idiotypic antibodies against the biologically active site of AFP. The specification does not describe any peptide that has the structure $CCRGDVLD_nX_mY$. According to the structure, the peptide must have an "X" (any hydrophobic amino acid) and an "Y" (any hydrophilic amino acid). The examples

disclosed, for example, SEQ ID NO: 1, has the sequence *Cys-Cys-Arg-Gly-Asp-Val-Leu-Asp-Cys*. This implies that both X and Y are absent or that X is a C or Y is a C and either X or Y is absent. However, according to the claim 2, index n is 1, 2 or 3 and index m is 1, 2 or 3. Thus, both X and Y must be present. The examples do not describe how to make and use the claimed peptide structure $CCRGDVLD_nX_mY$. Description of *Cys-Cys-Arg-Gly-Asp-Val-Leu-Asp-Cys* (SEQ ID NO: 1), Arg-Gly-Asp-Val-Leu-Asp (SEQ ID NO: 2), His-Gly-Asp-Leu-Leu-Glu (SEQ ID NO: 3), *Cys-Gly-Arg-Gly-Asp-Val-Leu-Asp-Cys* (SEQ ID NO: 4), *Cys-Cys-His-Gly-Asp-Leu-Leu-Glu-Cys* (SEQ ID NO: 5), *Cys-Gly-His-Gly-Asp-Leu-Leu-Glu-Cys*, and



are not sufficient to encompass other claimed peptide structure of the base claim that belong to the same genus. However, the specification does not provide for the peptides embraced by the broad generic or for the peptides which are embraced by at having 0, 1, 2, or 3 flanking cysteine residues at the N-terminus and 0, 1, 2 or 3 flanking cysteine residues at the C-terminus of the peptide.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the reference above and the high unpredictability and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to make peptide structures having $CCRGDVLD_nX_mY$, having a capability to regulate apoptotic cell death.

Conclusion

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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